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10/099,924	03/14/2002	Daniel Albert Wettstein	1909.03	2745

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/099,924
Filing Date: March 14, 2002
Appellant(s): WETTSTEIN ET AL.

Jay Z. Zhang
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 1, 2006 appealing from the Office action mailed January 23, 2006 (Advisory Action) and/or September 1, 2005 (Final Office Action).

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6168926	SYNDER	01-2001
6800737	ALTIERI	03-2004

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112, New Matter Rejection

Claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **THIS IS A NEW MATTER REJECTION.**

Claims 40(b), (ii); 43; 45(b),(c),(ii),(iii); 49; and 50 contain new matter. Sspecifically, claim 40 includes the recitations, " (b) a first polypeptide having...at least 80% identical to that..." and "(ii) a second polypeptide having...at least 80% identical to that ...". Claim 43 cites "...fragments of survivin comprises amino acid residues...47 to 99 of survivin." Claim 45 includes the recitations:

"(b) a survivin fragment containing a contiguous span of 10 amino acid residues..." ;

"(c) a first polypeptide having an amino acid sequence at least 90% identical to that..."'

"(ii) an HDLC1 fragment comprising a contiguous span of 10 amino acid residues..."; and

"(iii) a second polypeptide having an amino acid sequence at least 90% identical to that...". And claims 49 and 50 claims cite at least 80% and 90% identical to that of particular fragments defined by specific amino acid residues, respectively.

The specification seems to be remiss of amino acid residues 47 to 99 of survivin interacting with HDLC1, fragment thereof, or a polypeptide 80% or 90% identical to HDLC1. Likewise, it is unclear where in the specification Appellant have contemplated only 80%, 90% or a contiguous span of 10 amino acids of a first polypeptide, survivin interacting with at least 80%, 90% or a contiguous span of 10 amino acids of a second polypeptide. Appellant have not noted in the Remarks submitted April 4, 2005 and May 5, 2005 where support for these specific contemplations can be found in the disclosure. Accordingly, these claims contain new matter.

Claim Rejections - 35 USC § 112, Written Description

Claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Appellant broadly claims an isolated protein complex having a first protein, which is survivin, fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment which interacts with a second protein which is human cytoplasmic dynein light chain 1 (HDLC1) or fragment

thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment. The written description in this instant case only sets forth first protein, survivin which is 142 amino acids long (GenBank Accession number U75285) and second protein, HDLC1 which is an 89 amino acid protein (GenBank Accession number U32944), as well as the specific fragments cited in Table 1 on page 21. Therefore the written description is not commensurate in scope with the claims drawn to an isolated protein complex having less than 100% sequence identity to survivin or less than 100% sequence identity to specific fragments of survivin listed in Table 1 and less than 100% sequence identity to HDLC1 or less than 100% sequence identity to specific fragments of HDLC1 listed in Table 1. Furthermore, Appellant is only in possession of an isolated protein complex consisting of isolated protein complexes of survivin (amino terminus residues 3-99), (carboxy terminus residues 89-142) and core binding site residues 89-99 of survivin which specifically interact with HDLC1, see the specification, Table 1; page 23, lines 6-31; and page 24, lines 21-24. Appellant is not in possession of essentially any and all homologues, derivatives or fragments of the first and second proteins within an isolated protein complex or fusion protein. The homologues and derivatives more than likely comprise undefined amino acids that would not resemble the art known proteins, survivin and HDLC1 as defined by their corresponding GenBank Accession numbers.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "Appellant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Appellant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Appellant is not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Appellant is only in possession of the fragment species of survivin and HDLC1 listed in Table 1, see page 21. Appellant has characterized the 3 sets of bait/binding protein regions of survivin and its interacting partner, HDLC1 prey/interactor protein regions. Appellant is not in possession of unidentified and uncharacterized homologues, derivatives and fragments thereof of survivin and its interacting partner, HDLC1. Appellant is not permitted to claim all possible peptide combinations comprised within the claimed isolated protein complex or fusion proteins that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. As Appellant's claims are written they encompass variants, as well as sequences yet to be discovered.

There is no description of the sites at which variability may be tolerated. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. One skilled in the art cannot reasonably conclude that the Appellant had possession of the claimed invention at the time the instant application was filed.

Appellant's attention is directed to the Official Gazette, Volume 1242 published January 30, 2001. On page 1242 OG 174, column 1, section 2 "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice...". Appellant has not provided evidence substantiating they are in possession of the entire genus reading on polypeptides 80% or 90% sequence identical to survivin or HDLC1 and moreover fragments sharing 80% or 90% sequence identity to fragments of survivin comprising 97 and 53 residues long. This section of the OG clearly sets forth "where there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus." Information regarding how to make a variant or an assay for detecting the activity of a variant is not a showing of possession of the entire genus claimed. It is clear that the species identified in the specification attributing to the interaction between survivin and HDLC1 consists of critical structure as indicated in Appellant' specification, see page 23, lines 25-31.

There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Appellant is referred to the revised

interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, Enablement

Claims 40-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Appellant broadly claims an isolated protein complex having a first protein, which is survivin, fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment which interacts with a second protein which is human cytoplasmic dynein light chain 1 (HDLC1) or fragment thereof, 10 contiguous amino acid residues or polypeptide having at least 80%-90% sequence identity to survivin or survivin fragment. The wild type proteins are depicted in the GenBank Accession numbers referenced on page 21. The claims continue to encompass undefined and uncharacterized protein fragments, fusion proteins, peptides, homologues and derivatives.

And while one of ordinary skill in the art can theoretically produce all of these proteins with art known techniques it is burdensome to one of ordinary skill in the art to make and use these different combinations and thereafter determine their activity. Appellant's disclosure has not set forth any criteria as guidance to know which residues should be modified or deleted. Granted that is undue experimentation given that this

would require a level of ingenuity beyond what is expected from on of ordinary skill in the field. To further substantiate the Examiner's position Appellant was requested to review sequence 2 of U.S. Patent 6,168,926 (issued January 2, 2001). Sequence 2 is 100% sequence identical to HDLC1, however sequence 2 is not recognized as a HDLC1, but a rat protein inhibitor of nitric oxide, see sequence listing, columns 15-18. It is reasonable to those in the art high sequence identity cannot be used as the sole standard for the ability to use. And U.S. Patent number 6,800,737 (issued March 9, 2004) presents sequence 6,392, which is at least 82.5% sequence identical to survivin, however it is identified as an expressed sequence tag not completely identified or characterized.

There is no guidance of record setting forth the strategy of obtaining the broadly claimed isolated protein complex comprising survivin homologues, derivatives and fragments interacting with HDLC1 homologues, derivatives and fragments. The peptide art is unpredictable with regard to determine what peptides resulting form deletions, additions, mutations or analogues would be biologically active. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no

guidance as to which of the infinite possible choices is likely to be successful in making the complex and using the complex in the manner suggested by the specification.

From the analysis established above and of record it is clear that the predictability of changes to an amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed polypeptides in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which can be made in the protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

(10) Response to Argument

Claim Rejections - 35 USC § 112, New Matter Rejection

Appellant asserts the claim language the Examiner has noted to read on new matter is not so and addressed in their response dated November 1, 2005, see page 6 of the Appeal Brief. Appellant asserts they have pointed to numerous tracts of the specification that allegedly supports the specific portions of claims 40-50 that the Examiner has deemed uncorroborated by the disclosure. On page 6 of the Brief Appellant has reproduced their response of record in the Remarks submitted November 1, 2005, page 9.

Reviews by the Examiner of the particular sections of the specification Appellant has distinguished as supportive do not support the claims. For instance, page 17, lines 11-14 notes

> "a protein homologue of a native protein may have an amino acid sequence that is at least 50%, preferably at least 75%, more preferably at least 80%, 85%, 86%, 87%, 88% or 89%, even more preferably at least 90%, 91%, 92%, 93% or 94%, and most preferably 95%, 96%, 97%, 98% or 99% identical to the native protein."

This passage does not support a first polypeptide having an amino acid sequence at least 80% identical to a fragment of survivin that interacts with HDLC1 as listed in claim 40 (b), nor does it support claim 40 (ii). None of the disclosure reads on sequences of at least 80% sequence identity to fragments of survivin or HDLC1. Native proteins such as survivin or HDLC1 may have protein homologues of reduced sequence identity, *but not the fragments* of those native proteins.

Appellant also points out page 27, line 30-page 28, line 12 as supporting these claims, as well as claims 49 and 50, but this section of the specification reads on a protein complex comprising two interacting partners, which are a complete native survivin, a survivin homologue capable of interacting with, e.g., HDLCI, a survivin derivative, a derivative of the survivin homologue, a survivin fragment capable of interacting with HDLCI (survivin fragments) containing specific amino acid residues in Table 1 of the specification found on page 21.

Claim 43 cites "...fragment of survivin comprises amino acid residues...47 to 99 of survivin." Table 1 nor any other sections of the specification support this particular claim language citing these specific residues.

Fragment language found in the specification pointed out by Appellant on page 96, lines 23-25 reads on agents to be administered and

> "the protein fragment used is a fragment of an interacting protein member *having a length of less than 90%, 80%, more preferably less than 75%, 65%, 50%, or less than 40% of the full length of the protein member.*"

This passage speaks of fragments having 40%-90% less *length* than the full length wild-type protein. This does not read on at least 80% *sequence* identity to that of the wild-type protein. These are two different contemplations.

Likewise, contrary to Appellant's assertion, there is insufficient support found in the specification for "a survivin fragment containing a contiguous span of 10 amino acid residues", see claim 45. Page 97, lines 7-11 of the specification reads on an interacting protein (i.e. HDLC1) of survivin having a contiguous span of designated amino acids residues and not the survivin itself. The language herein is not commensurate. Accordingly, the rejection is maintained as new matter and not fully supported by the specification as filed.

Claim Rejections - 35 USC § 112, Written Description

Appellant reiterates the criteria for an Examiner to establish one skilled in the art could not reasonably conclude Appellant had possession of the invention at the time of filing, see bridging paragraph of pages 6 and 7 of the Brief. Appellant presents Federal Circuit case law, presents an analysis, which they regard as analogous to patent claims and USPTO guidelines for patent applications, see pages 8-11 of the Brief.

Appellant is reminded that Example 14 of the USPTO's Revised Interim Written Description Guidelines Training Materials is not binding law and should not be considered as information to support an argument.

The specification clearly identifies Appellant's possession of the fragment species of survivin and HDLC1 listed in Table 1, see page 21. As stated in the Final Office Action mailed November 1, 2005 Appellant has characterized 3 sets of bait/binding protein regions of survivin and its interacting partner, HDLC1 prey/interactor protein regions. Appellant is not in possession of unidentified and uncharacterized homologues, derivatives and fragments thereof of survivin and its interacting partner, HDLC1. Appellant has not exemplified support or contemplation for all the possible peptide combinations comprised within the claimed isolated protein complex or fusion proteins that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. As Appellant's claims are written they encompass variants, as well as sequences yet to be discovered. There is no description of the sites at which variability may be tolerated. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. One skilled in the art cannot reasonably conclude that the Appellant had possession of the claimed invention at the time the instant application was filed.

Appellant has not provided evidence substantiating they are in possession of the entire genus reading on polypeptides 80% or 90% sequence identical to survivin or HDLC1 and moreover fragments sharing 80% or 90% sequence identity to fragments of survivin or HDLC1. The Examiner reiterates page 1242 of the Official Gazette, Volume

1242 published January 30, 2001, column 1, section 2 wherein the criteria is clearly set forth "where there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus." Information regarding how to make a variant or an assay for detecting the activity of a variant is not a showing of possession of the entire genus claimed. It is clear that the species identified in the specification attributing to the interaction between survivin and HDLC1 consists of critical structure as indicated in Appellant's specification, see page 23, lines 25-31.

As far as comments on the patents by Invitrogen and a reportedly well-reasoned discussion of Example 14 by Appellant, Appellant is reminded each case or application has its own individuality and judgments and rejections are based on the particulars of each case. The rejection is maintained for the reasons of record and the analysis set forth herein.

Claim Rejections - 35 USC § 112, Enablement

Appellant avers the Examiner has failed "...to establish a prima facie case of nonenablement.", see page 13 of Brief, section 1. Appellant mischaracterizes the Examiner's rejection set forth in the Final Rejection asserting the Examiner presents to Appellant stringent means to obviate the instant rejection, see said section of Brief. The Examiner explicitedly stated in the Final Action, page 10, 2nd paragraph,

> "one of ordinary skill in the art can *theoretically* produce all of these proteins with art known techniques such as site-directed mutagenesis it would still be burdensome to one of ordinary skill in the art to produce all of these different combinations *and thereafter determine their activity*."

The Office has no requirement in the patent law requiring that an actual reduction to practice occur, however there must be an amount of direction or guidance presented in the specification and a reasonable showing of the breadth of the claims presented. Appellant's disclosure has not set forth any criteria as guidance to know which residues should be modified or deleted. There is undue experimentation presented given the breadth of the claims that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. The Examiner presented evidence substantiating the rejection. Sequence 2 of U.S. Patent 6,168,926 (issued January 2, 2001) is 100% sequence identical to HDLC1, however sequence 2 is not recognized as a HDLC1, but a rat protein inhibitor of nitric oxide, see sequence listing, columns 15-18. It is reasonable to those in the art high sequence identity cannot be used as the sole standard for the ability to use. And U.S. Patent number 6,800,737 (issued March 9, 2004) presents sequence 6,392, which is at least 82.5% sequence identical to survivin, however it is regarded as an expressed sequence tag not completely identified or characterized. It is clear from Appellant's claims they embody survivin and HDLC1 variants, as well as amino acid sequences derived from the said variants, which read on polypeptides other than survivin and HDLC1.

There is no guidance of record setting forth the strategy of obtaining the broadly claimed isolated protein complex comprising survivin homologues, derivatives and fragments interacting with HDLC1 homologues, derivatives and fragments. The peptide art is unpredictable with regard to determine what peptides resulting form

deletions, additions, mutations or analogues would be biologically active. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful in making the complex and using the complex in the manner suggested by the specification. Hence, the rejection is maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the Examiner in the Related Appeals and Interferences section of this Examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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8/16/06 cafree

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